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Latex allergy: diagnosis, testing, foods that cross react

12/8/2010

Q.

**First question: Are there any guidelines or procedures we could use to facilitate skin testing for latex allergy? We are aware there are no standardized skin tests for latex allergy, however, any insight would be appreciated.**

**Second question: How accurate are the Lab blood tests for latex allergy?**

**Last question: Are there any known foods that cross-react with latex allergies?**

**Thank you for your assistance.**

A.

Thank you for your recent inquiry.

Let me start first with the easiest question to answer. This relates to your inquiry as to which foods have been shown to cross-react with latex. These foods include the following: banana, potato, avocado, kiwi, chestnut, papaya, apples, peaches, plums, figs, grapes, melons, passion fruit, cherries, nectarines, pears, pineapple and strawberries, carrots, celery, raw potatoes, and tomatoes; chestnuts and hazelnuts.

The other two questions are far more difficult. I have copied below a number of abstracts from articles dealing with the issue of confirming the diagnosis of latex allergy by in vivo and in vitro tests. The answer to both of your questions related to diagnosis (protocol for skin testing, and the accuracy of in vitro tests) is embedded in these articles. I would specifically suggest the Hamilton RG, et al. article that appeared in The Journal of Allergy and Clinical Immunology in 2002. This article has specific suggestions as to testing, and also deals with the sensitivity and specificity of the various in vitro tests for latex allergy. One cannot answer the question regarding the accuracy of these tests because there are a number of tests available, and each one varies in their specificity and sensitivity as you will see from this article.

In addition, unfortunately, because we lack a standardized extract for testing, the sensitivity and specificity of skin tests and provocation tests using our only source of allergen (latex gloves) is also dependent upon the quantity of allergen in the glove itself and the specific tests that are employed.

As you will see when you look at the Hamilton article, there are several ways to do in vivo tests. In general, the in vivo tests that are employed, using gloves, are highly significant if positive, but cannot be trusted if negative. That is, they have a high specificity, but low sensitivity.

I am not aware of any true standard protocol, but I can share with you the tests that we perform in vivo. They are done in the following sequence:

We soak a latex glove in saline for one hour, and then do an epicutaneous test with the extract. If positive, we go no further. If negative, we then go to:

A wet latex glove is applied to the forearm for one-half hour. If this is a positive test, we go no further, but if negative, we go to:

We prick the skin through the wet latex glove.

We also perform, for corroborative purposes and to fortify the diagnosis, an in vitro test using the ImmunoCap. The specificity and sensitivity of this test is discussed in the Hamilton article.

Thank you again for your inquiry and we hope this response is helpful to you.

#### Articles:

J Allergy Clin Immunol. 2002 Aug;110(2 Suppl):S47-56.

Clinical and laboratory-based methods in the diagnosis of natural rubber latex allergy.

Hamilton RG, Peterson EL, Ownby DR.

Division of Allergy and Clinical Immunology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD 21224, USA.

Comment in: J Allergy Clin Immunol. 2003 Jun;111(6):1414; author reply 1414-6.

#### Abstract

The accurate diagnosis of hypersensitivity to natural rubber latex is the initial step in the effective management of individuals with latex allergy and in ensuring the quality of epidemiologic studies. The diagnostic algorithm used in the evaluation of an individual with suspected latex allergy begins with a comprehensive clinical history during which risk factors (atopy, food allergies, hand dermatitis) and temporal relationships between symptoms and natural rubber product exposure are identified. If type IV hypersensitivity is suspected because of the delayed nature (hours to days) and confinement of symptoms to the skin-latex product contact areas, patch testing can be conducted to confirm the presence of activated T cells with specificity for rubber chemicals. If type I hypersensitivity is suspected because of ocular, upper and lower airway, and/or systemic symptoms that have rapid onset (minutes) after a definable latex exposure, a confirmatory skin or blood test for IgE antibody may be conducted to verify a state of sensitization within the individual. The definitive diagnosis would then be made only after consideration of the individual's clinical history and confirmatory in vivo and/or in vitro laboratory test results. If discordance remains between highly convincing latex-associated symptoms as identified in the history and repetitively negative confirmatory IgE antibody test results, then one of several types of in vivo provocation tests may be performed for adjudication. This overview examines the current state of the art in both in vivo and in vitro diagnostic methods for latex-specific IgE antibody detection in skin and blood. The performance, advantages, and limitations of each diagnostic method are compared.

PMID: 12170243 [PubMed - indexed for MEDLINE]

Allergol Int. 2010 Sep;59(3):305-8. Epub 2010 Jul 25.

Pitfalls in the diagnosis of latex allergy. Khan S, Holding S, Doré P, Sewell C.

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#### Abstract

**BACKGROUND:** Screening patients for latex allergy prior to surgery is an important but intensive procedure. The appropriate testing strategy for diagnosing latex (*Hevea brasiliensis*) allergy involves in-vitro specific IgE or skin prick testing. The sensitivity and specificity of both tests are influenced by patient-specific factors or manufacturing processes that alter the clinically relevant allergens in skin testing solutions.

**METHODS:** Total IgE and latex-specific IgE testing was introduced as a screening test. Skin prick testing was done on patients with a high probability of latex allergy and negative specific IgE with total IgE <100 kU/L. SDS-PAGE was done on the non-ammoniated latex (NAL) and newly introduced ammoniated latex (AL) reagents for the clinically relevant allergens.

**RESULTS:** 51 patients had a total IgE <100 (range, 2.8-99.0 kU/L), and 10% had a positive skin test. 60% of positive skin tests would have been missed with lower total IgE

cut-offs of 50 kU/L (6% of referrals). SDS-PAGE of the NAL solution showed 3 prominent bands with molecular weights of approximately 20, 24 and 42 kDa that correlated with Hev b 6, Hev b 3 and Hev b 7/13, respectively. In contrast, the AL solution showed 3 very faint higher molecular weights bands that did not correlate with clinically relevant antigens.

**CONCLUSIONS:** Increasing the cut-off value of total IgE for allergen-specific IgE testing increased the sensitivity of the specific IgE test. The NAL reagent had a greater number of clinically significant allergens at higher concentrations than AL, which may have implications for the clinical sensitivity of the newer AL reagent.

Clin Exp Allergy. 2007 Sep;37(9):1349-56.

Percutaneous reactivity to natural rubber latex proteins persists in health-care workers following avoidance of natural rubber latex. Smith AM, Amin HS, Biagini RE, Hamilton RG, Arif SA, Yeang HY, Bernstein DI. Department of Internal Medicine, Division of Allergy/Immunology, University of Cincinnati, Cincinnati, OH, USA. sa6@email.uc.edu  
Abstract

**BACKGROUND:** Long-term avoidance of natural rubber latex [*Hevea brasiliensis* (Hev b)] is currently recommended for health-care workers (HCWs) with established natural rubber latex (NRL) allergy. Percutaneous sensitivity to eight Hev b NRL allergens was evaluated in HCWs in 2000. To date, no studies have evaluated the longitudinal effects of NRL avoidance on percutaneous sensitivity to NRL allergens.

**OBJECTIVE:** The aims of this study were to evaluate changes in percutaneous reactivity to non-ammoniated latex (NAL) and NRL allergens in HCWs 5 years after a recommendation to avoid NRL and to evaluate factors that predict the persistence of in vivo sensitivity to NAL and NRL allergens.

**METHODS:** Skin prick testing was performed with NAL, seven NRL allergens (Hev b 1, 2, 3, 4, 6.01, 7.01, and 13), and recombinant Hev b 5 (rHev b 5) in 34 HCWs who were initially evaluated in 2000 for occupationally related NRL allergy. Serial 10-fold dilutions of NAL and NRL allergens were employed in skin testing. Sera from the HCWs were assayed for latex and enhanced latex (rHev b 5-enriched allergosorbent)-specific IgE antibodies using the ImmunoCAP assay.

**RESULTS:** The prevalence of work-related symptoms significantly decreased between 2000 and 2005 with avoidance of NRL ( $P < 0.05$ ). A  $\geq 100$ -fold reduction in percutaneous sensitivity to Hev b 2 and Hev b 7 was less likely in those with prior history of systemic reactions to NRL ( $P = 0.0053$ ), reported history of reaction to cross-reactive foods ( $P = 0.014$ ), continued local reactions to NRL gloves ( $P < 0.0001$ ), or high NRL glove exposure since the initial study ( $P = 0.0075$ ). The diagnostic sensitivity and specificity of the latex-specific IgE serology was 54% and 87.5%, respectively, in comparison with NAL skin tests. The addition of rHev b 5 to the ImmunoCAP (enhanced latex) allergosorbent altered the diagnostic sensitivity and specificity of the ImmunoCAP to 77% and 75%, respectively.

**CONCLUSION:** While symptoms may resolve quickly with NRL avoidance therapy, detectable IgE indicating continued sensitization remains beyond 5 years, and thus continued avoidance of NRL should be recommended

Int J Immunopathol Pharmacol. 2010 Apr-Jun;23(2):543-52.

Challenge tests in the diagnosis of latex allergy. Nucera E, Pollastrini E, Sabato V, Colagiovanni A, Aruanno A, Rizzi A, Buonomo A, Pecora V, Lombardo C, Astorri AL, Rossi G, Patriarca G, Schiavino D. Allergy Unit, Università Cattolica del Sacro Cuore, Policlinico A. Gemelli, Rome, Italy.

Abstract

The aim of this study is to evaluate the sensitivity, specificity and safety of challenge tests and their usefulness in the diagnosis of latex allergy. Forty adult subjects (F/M = 34/6, aged 18-66 yrs) with a history of adverse reactions after latex exposure and positive prick test and/or specific IgE to latex were enrolled. They were compared with 20 control subjects. They underwent provocative (cutaneous, mucous-oral, sublingual, conjunctival,

nasal, bronchial, vaginal) tests. Symptoms and drug scores were recorded for each patient during challenges. All patients reacted to at least one of the following: cutaneous, nasal and conjunctival tests. No systemic reactions requiring epinephrine occurred. Of the challenges, the vaginal test resulted as the safest, but it had low sensitivity and many limits related to the procedure. According to our data, bronchial and nasal tests had the highest sensitivity (76% and 82% respectively), and were more precise than other tests in determining latex exposure and symptoms, but the bronchial test also presented the highest rate of risk. Mucous and cutaneous tests resulted as the most reliable. For all the tests, specificity and positive predictive value were 100%. All control subjects resulted negative to all challenges. There were no statistically significant changes in skin and serologic tests between the first and second visits. Correlations between MIS and skin tests and between MIS and serum tests were not found. Challenges can be considered safe diagnostic procedures. Tests that most faithfully reproduce natural exposure, on the basis of a patient's history, are preferable

J Allergy Clin Immunol. 1997 Nov;100(5):618-23.

Latex-specific IgE, skin testing, and lymphocyte transformation to latex in latex allergy. Ebo DG, Stevens WJ, Bridts CH, De Clerck LS. Department of Immunology, Allergology, and Rheumatology, University of Antwerp (UIA), Belgium.

#### Abstract

**BACKGROUND:** This study was designed to determine the discriminative value of latex-specific IgE tests, latex skin tests, and lymphocyte transformation tests (LTTs) to latex in 38 patients with latex allergy (12 nonatopic and 26 atopic) and 44 control subjects (24 nonatopic and 20 atopic). We also evaluated the recommended positive cutoff (i.e., 0.35 kU/L) of both in vitro latex-IgE tests.

**METHODS:** Latex-specific IgE levels were determined by the Immuno-CAP (Upjohn-Pharmacia) and the ALaSTAT-RIA (Diagnostic Products Corp.) assays. Skin tests and LTFs were performed with a nonammoniated latex extract (DPC). Sensitivities and specificities were defined according to the 95th percentile value of nonatopic control subjects. For the in vitro IgE tests, sensitivity and specificity were also calculated by using the proposed positive threshold of 0.35 kU/L. Sensitivities and specificities of both cutoffs were compared.

**RESULTS:** Compared with a clinical history of latex allergy and according to the 95th percentile value of nonatopic control subjects (0.44 kU/L), latex-specific IgE determined by the Immuno-CAP assay achieved a sensitivity of 97% and a specificity of 86%. For the ALaSTAT-RIA assay, with 0.54 kU/L as the 95th percentile threshold value in nonatopic control subjects, sensitivity was 100%, and specificity was 83%. According to the threshold value of 0.35 kU/L, a sensitivity of 97% and a specificity of 83% for the Immuno-CAP assay and a sensitivity of 100% and a specificity of 33% for the ALaSTAT-RIA assay were observed. The latex skin test reached a sensitivity of 97% and a specificity of 100%. The LTF to latex showed a sensitivity of 39% and a specificity of 95%. No relation between symptoms and latex-specific IgE tests, latex skin tests, or LTTs was found.

**CONCLUSIONS:** Our results confirm that latex skin tests and latex-specific IgE assessments are sensitive and specific methods for establishing the diagnosis of latex allergy, although the specificity of the ALaSTAT-RIA assay was very low when interpreted according to the threshold of 0.35 kU/L. The LTT to nonammoniated latex is too insensitive for diagnosis of allergy to latex. This reemphasizes that in order to evaluate the sensitivity and specificity of diagnostic procedures, one should always include an appropriate control group.

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Sincerely,  
Phil Lieberman, M.D.

Key Words: latex allergy, serologic testing for latex allergy, skin test for latex allergy, foods cross reacting with latex

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